Abstract:

Disclosed are two new crystalline forms, δ and ϵ , of perindopril erbumine. Those forms are suitable as therapeutic active substances for medicaments for the treatment of cardio-vascular diseases, especially high blood pressure and heart failure. The ϵ crystalline form is obtained in the crystallisation of perindopril erbumine at from 30 to 45°C, preferably from 34 to 45°C, from MTBE containing from 1.5 to 2.5 % (v/v) water; the crystallisation is advantageously carried out with stirring. If the water is then removed, advantageously by azeotropic distillation, preferably at from 35 to 37°C, and stirring is then continued for at least 15 h at from 30 to 45°C, preferably from 35 to 37°C, the ϵ crystalline form is converted to the δ crystalline form. The δ crystalline form can also be obtained by stirring the α or β crystalline form at from 33 to 38°C in tert.-butyl methyl ether containing from 0.9 to 1.4 % (v/v) water with seeding with the δ crystalline form at from 28 to 35°C in tert.-butyl methyl ether containing from 0.9 to 1.4 % (v/v) water with seeding with the ϵ crystalline form; or by stirring the ϵ or ϵ crystalline form at from 35 to 38°C in tert.-butyl methyl ether containing from 0.9 to 1.4 % (v/v) water with seeding with the ϵ crystalline form; or by stirring the ϵ or ϵ crystalline form at from 35 to 38°C in tert.-butyl methyl ether containing from 1.5 to 2.0 % (v/v) water.